delivery system of the invention results in increased efficacy of intracellular delivery of such agents, bypassing the *endocytotic* pathway of intracellular delivery while at the same time minimizing the toxicity of the delivery system towards the recipient cells. (See para. [0019].) Furthermore, Torchillin et al. discloses that the transfer of the whole complex through the cell membrane is *mediated by the transducing polypeptides*. (See para. [0028].)

Admitting that Torchillin et al. does not disclose PE, the Examiner refers to WO 85 as disclosing an acid induced liposome fusion method wherein the presence of PE in the liposome enhances fusion of the liposome. WO 85 notably discloses that *endocytosis* of liposomes is primarily responsible for liposome uptake. (See Page 6, lines 10-11.) Further still, WO 85 discloses that in the case of liposome fusion mediated by proteins, e.g. serum albumin, clathrin and viral glycoproteins, it is clear that the protein conformational change is the primary driving force for fusion. In the invention of WO 85, the driving force comes from the lipid itself. (See Page 5, lines 3-10.) To this end, the purpose for adding PE into the invention of PE is to greatly enhance acid induced liposome fusion.

Summarizing the differences, Torchillin et al. discloses a polypeptide lipid vesicle complex, WO 85 discloses a liposome only, Torchillin et al. discloses bypassing the endocytotic pathway, WO 85 discloses liposome uptake is via endocytosis, Torchillin et al. discloses the polypeptide mediates the transfer through the cell, WO 85 discloses the driving force comes from the lipid. Based on the differences, two conclusions are inevitable: (1) that the method of delivery of Torchillin et al. and WO 85 are different, and (2) that PE only serves to enhance the method of WO 85. Accordingly, there is no apparent reason to include PE into the polypeptide lipid complex of Torchillin et al. since nothing suggests that it would have the intended effect as it did in WO 85, nor does PE appear to be necessary or desirable in the complex described by Torchillin et al. because the mechanisms of Torchillin et al. and WO 85 are different.

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Accordingly, it cannot be concluded that the combination of the teachings of WO 85 with the teachings of Torchillin et al. would have led one skilled in the art to produce the invention of Claim 1. Therefore, the rejection of Claims 1-5, 7-12, and 18-20 should be reversed.

The Rejection of Claims 1-12 and 18-20 Under 35 U.S.C. § 103(a)

Claims 1-12 and 18-20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Torchillin in combination with WO 85/04880, and further in view of U.S. Patent No. 5,902,802 (Heath).

The reasons why Claim 1 is not obvious in view of Torchillin et al. and WO 85 is fully discussed above. Heath is cited merely for disclosing ergo sterol. Therefore, even considering the teachings of Heath with the teachings of Torchillin et al. and WO 85 does not render Claim 1 obvious.

Therefore, the rejection of Claims 1-12 and 18-20 should be reversed.

The Rejection of Claims 13-15 and 18 Under 35 U.S.C. § 103(a)

Claims 13-15 and 18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Torchillin in combination with WO 85/04880 in view of Heath, and further in view of U.S. Patent Application Publication No. US 2002/0081633 (Kapeller-Libermann).

The reasons why Claim 1 is not obvious in view of Torchillin et al. and WO 85 is fully discussed above. Kapeller-Libermann is cited merely for disclosing the delivery of phosphodiesterase to cells in vitro as well as in vivo. Therefore, even considering the teachings of Kapeller-Libermann with the teachings of Torchillin et al. and WO 85 does not render Claim 1 obvious.

Therefore, the rejection of Claims 1-12 and 18-20 should be reversed.

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The Rejection of Claims 16-18 Under 35 U.S.C. § 103(a)

Claims 16-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Torchillin in combination with WO 85/04880 in view of Heath, and further in view of U.S. Patent Application Publication No. US 2002/0156259 (Conklin).

The reasons why Claim 1 is not obvious in view of Torchillin et al. and WO 85 is fully discussed above. Conklin is cited merely for disclosing the delivery of deaminase. Therefore, even considering the teachings of Conklin with the teachings of Torchillin et al. and WO 85 does not render Claim 1 obvious.

Therefore, the rejection of Claims 16-18 should be reversed.

CONCLUSION

In view of the foregoing remarks, applicant submits that Claims 1-20 are in condition for allowance. If the Examiner has any further questions or comments, the Examiner is invited to contact the applicant's attorney at the number provided below.

Respectfully submitted,

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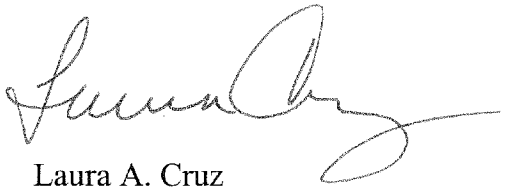

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